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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/637,190	08/08/2003	Curt Dale Haffner	PU3616US2	5880

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EXAMINER	
ANDERSON, REBECCA L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/637,190	HAFFNER ET AL.	
	Examiner	Art Unit	
	Rebecca L Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,20 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,20 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

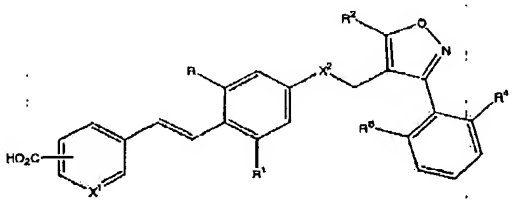
Claims 16, 20 and 36 are currently pending I the instant application and are rejected.

Election/Restrictions

Applicant's election without traverse of Group III drawn to methods of lowering serum triglycerides in a mammal and the further election of the single compound GW4064 in the reply filed on 27 April 2004 is acknowledged.

The election of the compound GW4064 has resulted in the following for search and examination:

The elected invention for search and examination is the method of lowering serum triglycerides in a mammal comprising administering to a mammal in need thereof an effective serum triglyceride lowering amount of a nonsteroidal agonist for Farnesoid X Receptor of the following formula:



Wherein X1 is CH or N; X2 is O or NH; R and R1 are independently H, lower alkyl, halogen, or CF3; R2 is lower alkyl; R3 and R4 are independently H, lower alkyl, halogen, CF3, OH, O-alkyl, or O-polyhaloalkyl.

The remaining subject matter of claim 20 that is not drawn to the above elected invention stands withdrawn under 37 CFR 1.142(b) as being for non-elected subject The remaining methods which are not within the elected invention, which are

independent and distinct from the elected invention and do not have unity with the elected invention and therefore are withdrawn by means of a restriction requirement within the claims are, for example, methods of lowering serum triglycerides in a mammal by administering other than the compound as found in claim 36.

The above mentioned withdrawn methods which are withdrawn from consideration as being for nonelected subject matter differ materially in structure and composition in the products utilized in the elected invention. The withdrawn methods utilize products which differ materially in structure and composition from those of the elected invention. Therefore, again, the methods which are withdrawn from consideration as being for non-elected subject matter differ materially in structure an composition of the products utilized and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter.

The withdrawn methods are independent and distinct from the elected invention and do not have unity with the elected compound and are therefore withdrawn by means of a restriction requirement within the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 20 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the treatment of atherosclerosis does not

reasonably provide enablement for the treatment of all disease mediated by modified lipid levels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention in claims 16, 20 and 36 is the lowering of serum triglycerides in a mammal by administering the elected invention for the treatment of any disease associated with modified lipid levels.

The state of the prior art

The state of the prior art is that farnesoid X receptor is a bile acid-activated transcription factor that is a member of the nuclear hormone receptor superfamily. The

farnesoid X receptor functions as a bile acid sensor coordinating choleterol metabolism, lipid homeostasis and absorption of dietary fats and vitamins.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of diseases characterized by modified lipid levels, whether the disease included by this claim are affected by a compound which lowers serum triglycerides would affect the possible treatment of any disease.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula (I) due to the unpredictability of the role of serum triglycerides and the unpredictability as to what diseases are encompassed by the instant claims. The nature of the pharmaceutical arts is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities and which diseases would be affected by this activity. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is the binding assays on pages 11-18.

The presence or absence of working examples

There are no working examples in the instant specification for the treatment of any disease applicant considers characterized by modified lipid levels. The compounds which are disclosed in the specification have no pharmacological data regarding the treatment of any of the diseases and fails to provide working examples as to how the diseases are correlated the lowering of serum triglycerides

The breadth of the claims

The breadth of the claims encompasses the treatment of any disease characterized by lowered serum triglycerides,

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases characterized by the modification of lipid levels would benefit from lowered serum triglycerides and would furthermore then have to determine what compounds of the elected invention would provide treatment of what, if any, disease.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to

determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus the specification fails to provide sufficient support for the broad use of the compound of the formula (I) for the method of lowering serum triglycerides for the treatment of any disease characterized by a modification of lipid levels. As a result necessitating one of skill to perform an exhaustive search in order to practice the claimed invention.

Genentech Inc.v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vaque intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and in re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation with no assurance of success. This rejection can be overcome by amending the claims to include only method of lowering serum triglycerides for the treatment of atherosclerosis The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically claim 16 recites wherein said FXR agonist is

GW4064 which is not a universally recognized chemical name. While applicant may be his or her own lexicographer, under modern claim practice, claims must stand alone to define the invention and incorporation into claims by express reference to specification and/or drawings is not permitted. Since GW4064 is not a universally recognized chemical name, one must refer back to the specification to determine what applicant is claiming by referring to the chemical structure on page 7 of the instant specification.. It is suggested that applicant insert the chemical structure of GW4064 into the claim

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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